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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,179	07/02/2003	Roland Kreutzer	14174-104USS/RIB001.3USD4	5239

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EXAMINER

VIVLEMORE, TRACY ANN

ART UNIT PAPER NUMBER

1635

DATE MAILED: 01/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/612,179	KREUTZER ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 November 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The finality of the previous office action is withdrawn in view of the following new rejections.

Specification

The previous objections to the specification have been overcome by the amendments submitted August 4, 2005.

Priority

Based on the presence of new matter, the priority date for this application is the instant filing date, July 2, 2003.

Response to arguments- Claim Rejections - 35 USC § 112

Claims 4-9 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record set forth in the office action mailed July 13, 2005.

Applicant's arguments in the appeal brief filed November 4, 2005 are not persuasive with regard to the new matter rejection. Applicant states there is clear support for "isolated dsRNA of 15-49 base pairs composed of two separate strands either with or without an additional chemical linkage" and that "the examiner does not seem to disagree with this position." The examiner does disagree with this, neither the non-final nor the final rejection addresses whether the original claim range is supported.

In fact, both of the previous office actions state that the sole contemplation of the use of a 21mer is as a linked duplex.

Applicant points to line 26 of page 4 as providing support that the dsRNA of the invention is composed of separate strands. This argument is not persuasive because this statement refers to "a region II which is complementary within the double-stranded structure is formed by two separate RNA strands". While the specification refers to regions I and II there is no disclosed relationship between the two regions and it is unknown what region II is complementary to. The statement that region II is complementary within the double-stranded structure could be interpreted as region II being self-complementary.

Applicant also states there is nothing in the example that suggests the only way that applicant viewed their invention is as chemically linked molecules and that the conclusion statement is simply a statement that the experiment worked. The examiner disagrees that the conclusion is a simple statement of an experiment's success, the final sentence of the example states: "...even shorter dsRNAs can be used for specifically inhibiting gene expression in mammals when the double strands are stabilized by chemically linking the single strands". This implies the inventors believed that stabilization of the shorter dsRNAs is a requirement.

Applicant's arguments with regard to the findings of *In re Wertheim* are not persuasive because the examiner is not familiar with the prosecution history of the *Wertheim* application and thus is unaware of whether limitations present in the exemplified compounds were ever present in the claims.

Applicant states on page 8 of the appeal brief that "the pertinent feature of length, 15-21 nucleotides, is distinct from and separate from the other disclosed limitation, such as linked versus non-linked". The examiner agrees; the length limitation finds support in the specification, the limitation that the strands are non-linked does not.

Response to arguments - Claim Rejections - 35 USC § 102

Claims 4-9 remain rejected under 35 U.S.C. 102(b) as being anticipated by Fosnaugh et al. (US 2003/0143732).

Because applicant's arguments with regard to new matter are not persuasive, the priority date of the instant application remains July 2, 2003 and the reference of Fosnaugh et al. is a proper prior art reference.

New Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 4 and 6-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Crooke (US 6,107,094).

The claims are directed to double stranded RNAs that are 15-21 nucleotides in length that specifically inhibit the expression of a mammalian target gene. The RNAs may be modified to be resistant to RNA degradation and may consist of two strands that are fully complementary to each other.

Crooke discloses in example 27-a at column 50 (see also table 1) fully complementary double stranded RNAs 18 and 20 nucleotides in length targeted to either Ha-ras or C-raf. These sequences are complementary to less than the full length of an RNA transcript and do not comprise a full length transcript. Crooke further discloses that the double stranded RNAs are modified with phosphorothioates and are nuclease resistant. Crooke does not disclose that these RNAs will inhibit gene expression but since the prior art meets all structural limitations of the claims it would, absent evidence to the contrary, be expected to inhibit gene expression

Thus, Crooke discloses all limitations of and anticipates claims 4 and 6-9.

Claims 4-6 and 8 are rejected under 35 U.S.C. 102(e) as being anticipated by Fire et al. (US 6,506,559, cited on IDS), as evidenced by Zhang et al. (Cell 2004, vol. 118, pages 57-68).

The claims are directed to double stranded RNAs that are 15-21 nucleotides in length that specifically inhibit the expression of a mammalian target gene wherein one strand is complementary to less than the full-length of a target gene.

Fire et al. disclose that double-stranded RNA causes potent and specific RNA interference and that double-stranded RNA is substantially more effective at producing interference than either strand individually. Fire et al. disclose that one strand of the RNA is complementary to the target gene. Fire et al. further disclose that this effect can be used to inhibit any target gene, including mammalian genes. As evidenced by the post-filing art of Zhang et al., Dicer is a multidomain ribonuclease that processes long dsRNAs to fragments of 15-21 nucleotides during RNA interference. Although Fire et al. are silent as to the cleavage of long dsRNAs into double stranded duplexes 15-21 nucleotides in length, the long dsRNA molecules disclosed by Fire et al. are necessarily cleaved into such duplexes. As stated in the MPEP (see MPEP 2112), something that is old does not become patentable upon the discovery of a new property. The claiming of an unknown property which is inherently present in the prior art does not necessarily make the claim patentable. There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of the invention, but only that the subject matter is in fact inherent in the prior art reference. This inherency argument is bolstered by *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67USPQ2d 1664, 1668 (Fed. Cir. 2003). Inherent anticipation does not require recognition in the prior art. Since Fire et al. teach administering dsRNA and the resultant RNA interference, and it has since been discovered that this effect is mediated by the activity of Dicer, which cleaves long dsRNA into fragments that are 15-21 nucleotides long, the teachings of Fire et al. anticipate the instant invention. Furthermore, see *Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 970, 58 USPQ2d

1865 (Fed. Cir. 2001), "a limitation or the entire invention is inherent and in the public domain if it is the "natural result flowing from" the explicit disclosure of the prior art".

This is considered to inherently anticipate the compound even though the compound's existence was not known.

Therefore, the invention of claims 4-6 and 8 is anticipated by Fire et al., as evidenced by Zhang et al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Examiner
Art Unit 1635

TV
January 17, 2006


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PATENT EXAMINER